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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ARIANI, KADE	

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,678	HU ET AL.	
	Examiner	Art Unit	
	KADE ARIANI	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 11-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 11-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on April 29, 2010, has been received.

Claims 8 and 9 have been cancelled.

Claims 1-7 and 11-47 are pending in this application and were examined on their merits.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/29/2010 has been entered.

Applicant's arguments with respect to claims 1-7, and 11-47 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, and 29-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The added material which is not supported by the original disclosure is as follows:

In claims 1 (line 7), 29 step c) (lines 4-5) and 41 (lines 4-5) the recitation "substantially free from a core-shell polymer configuration".

Because the specification while provides support for IPN nanoparticles with core-shell polymer structure, and preparing the IPN nanoparticles particles with core-shell polymer structure (see for example page 18 0056). It does not provide support for IPN nanoparticles, IPN nanoclusters, and preparing IPN nanoparticles and nanoclusters which are substantially free from a core-shell polymer configuration.

Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP § 2163.06.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, and 29-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 29 and 41 the recitation "substantially free of core-shell polymer configuration" is indefinite because it is unclear how small the amount of core-shell polymer configuration must be present in the IPN nanoparticles for the IPN nanoparticles to be considered substantially free of core-shell polymer configuration.

In claim 29 step a) the recitation "providing a dispersion of IPN nanoparticles" is vague and indefinite because is not exactly clear how the dispersion of IPN nanoparticles is provided and what dispersion (e.g. an aqueous dispersion?) is being encompassed with this recitation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7 and 11-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over of Jones et al. (Macromolecules, 2000, Vol. 33, p.8301-8306) in view of Gan et al. (J Am. Chem. Soc., 2001, Vol. 123, p.7511-7517) and Kurisawa et al. (Journal of

Controlled Release, 1998, Vol. 54, p.191-200) and further in view of Cai et al. (Journal of Applied Polymer Science, 2002, Vol. 83, p.169-178).

Claims 15-28 are drawn to a method of preparing an interpenetrating polymer network (IPN) of monodispersed nanoparticles, comprising providing a first mono-dispersed polymer nanoparticles prepared by mixing first monomer, a surfactant, a first cross linking agent, and first initiator at a first temperature, wherein the first polymer has a low critical solution temperature of between 28ºC and 45ºC, the first polymerization temperature is above the LCST of the first monodispersed polymer: adding to the first mono-dispersed polymer a second monomer, a second cross linking agent, a second initiator and an activator, forming a nanoparticle solution wherein the nanoparticle solution is an aqueous solution, mixing the nanoparticles solution for a period of time at a second temperature, wherein the second temperature is below the low critical solution temperature of the first monodispersed polymer, isolating the IPN nanoparticles, (wherein the first monomer, the first cross linking agent, the second monomer, and the second cross linking agent are substantially free from dissolved oxygen gas and the first wherein the first polymer forms a first polymer network which interpenetrates a second polymer network formed by the second polymer, mixing the isolated IPN nanoparticles with a biologically active material at a third temperature, the biologically active material is a drug, wherein the third temperature is below a gelation temperature (Tg) of the IPN nanoparticles in a n aqueous mixture, (and wherein above the Tg the first polymer network consists of cross-linked polymer chains inside each nanoparticle, and the second polymer network consist of a cross-linked system of the nanoparticles), wherein

the Tg is about 33ºC, wherein the first polymer comprises poly (-N-isopropylacrylamide), the second polymer comprises poly (acrylic acid), the first cross linking agent comprises N, N'-methylenebisacrylamide, potassium persulfate, ammonium persulfate, the surfactant comprises SDS, and TEMED (activator), the IPN of nanoparticles hydrodynamic radius is in the range of 75 nm to about 200 nm, period of time is less than 130 minutes, is about 120 minutes, the first temperature is 70°C, and the second temperature at about 21°C.

Claims 1-7, and 11-14 are drawn to an aqueous dispersion of hydrogel nanoparticles comprising, interpenetrating polymer network (IPN) nanoparticles, wherein each IPN nanoparticles comprises a first polymer network interpenetrating a second polymer network, and an aqueous medium, wherein the first polymer comprises poly (-N-isopropylacrylamide), the second polymer comprises poly (acrylic acid), wherein the IPN nanoparticles are substantially free of a core-shell polymer configuration, and the aqueous dispersion of hydrogel nanoparticles can undergo a reversible gelation in response to a change in stimulus applied thereon, wherein the aqueous dispersion of hydrogel nanoparticles further comprising a biologically active material, a drug, wherein the stimulus is temperature, wherein the temperature change above a gelation temperature (Tg) induces a volume phase transition of the IPN nanoparticles, resulting in an inverse thermo-thickening property of the aqueous dispersion of hydrogel nanoparticles, (and wherein above the Tg the first polymer network consists of cross-linked polymer chains inside each nanoparticle, and the second polymer network consist of a cross-linked system of the nanoparticles), wherein

the inverse thermo-thickening property is a transformation from a low viscous fluid to a gel when heated above the Tg, the Tg is about 34ºC, the first polymer comprises poly (-N-isopropylacrylamide), the second polymer comprises poly (acrylic acid), the IPN nanoparticles have a uniformed sized hydrodynamic radius, the average hydrodynamic radius is in the range of 75 nm to about 200 nm, wherein the weight ratio of the first polymer and the second polymer in IPN nanoparticles is about 1:1.88, and total polymer concentration from about 1.25 wt% to about 5.25 wt% in distilled water.

Jones et al. teach a method of preparing an interpenetrating polymer network of nanoparticles, comprising providing a first polymer nanoparticles prepared by mixing first monomer, a surfactant, a first cross linking agent, and first initiator at a first temperature (p.8301 2nd column 3rd and 4th paragraphs and p.8302 1st column 1st paragraph, p.8302 1st column end paragraph lines 1-3 and 16), adding to the first polymer nanoparticles a second monomer, a second cross linking agent, a second initiator and an activator, forming a nanoparticle solution wherein the nanoparticle solution is an aqueous solution, mixing the nanoparticles solution for a period of time at a second temperature to form the IPN nanoparticles, isolating the IPN nanoparticles (p.8302 1st column 1st , 2nd and 3rd paragraphs), wherein the first monomer, the first cross linking agent, the second monomer, and the second cross linking agent are substantially free from dissolved oxygen gas (degassing under vacuum and purging with nitrogen) (p.8302 1st column 1st paragraph line 7-8), wherein the first polymer has a low critical solution temperature of 38 ºC (between 28ºC and 45ºC) (p.83 03 2nd column 2nd paragraph lines 5-6), polymerization temperature 70 ºC (is above the LCST of the

first polymer) (p.83 01 1st column end paragraph last line). Jones et al. further teach the first polymer comprises poly (-N-isopropylacrylamide) (Tg is about 34ºC), the second polymer comprises poly (acrylic acid) or AAc (p.8302 1st column 2nd paragraph line 2), the period of time is 30 minute plus 45 minutes (less than 120 minutes) (p.8302 1st column 1st paragraph line 13-15), and the average hydrodynamic radius of the nanoparticles is in the range of 75 nm to about 200 nm (p.8302 2nd column Figure 2. radius vs. Temp graph, b. Y-axis, radius of particles 80-200 nm).

Jones et al. also teach an aqueous dispersion of hydrogel nanoparticles comprising, interpenetrating polymer network (IPN) nanoparticles, wherein each IPN nanoparticles comprises a first polymer network interpenetrating a second polymer network, and an aqueous medium, wherein the first polymer comprises poly (-N-isopropylacrylamide), the second polymer comprises poly (acrylic acid) or AAc (p.8302 1st column 2nd paragraph line 2), and the aqueous dispersion of hydrogel nanoparticles can undergo a reversible gelation in response to a change in stimulus applied thereon, wherein the stimulus is temperature, wherein the temperature change above a gelation temperature (Tg) induces a volume phase transition of the IPN nanoparticles (thermally induced volume phase transition) (Abstract), resulting in an inverse thermo-thickening property of the aqueous dispersion of hydrogel nanoparticles, wherein the inverse thermo-thickening property is a transformation from a low viscous fluid to a gel when heated above the Tg (about 34ºC) (it must be noted that poly (-N-isopropylacrylamide) hydrogels undergoes a reversible volume phase transition at 32ºC, see Cai et al. (p.169 1st column lines 10-14), the IPN nanoparticles have an average hydrodynamic radius is

in the range of 75 nm to about 200 nm (p.8302 2nd column Figure 2. radius vs. Temp graph, b. Y-axis, radius of particles 80-200 nm), and 5% total polymer concentration (about 1.25 wt% to about 5.25 wt) (p. 8302 2nd column end paragraph lines 3), Jones et al. further teach wherein the first polymer and the second polymer in IPN nanoparticles have weight ratio of 9:1 (p.83 02 1st column 1st paragraph line 2).

Jones et al. also teach change in the particle size of the aqueous dispersion around 30 nm (at pH 6.5) when it is heated from below a volume phase transition temperature to above a volume transition temperature (about 34℃), the magnitude of the particle (p. 8304 Figure 5, Deswelling curves for particle at pH 6.5, the 1st curve on the top, radius change around 34℃, decrease in the magnitude of the particle size change, and the temperature on y-axis of the graph, and p. 8303 2nd column 3rd paragraph lines 13-15).

Jones et al .do not teach wherein the IPN nanoparticles are substantially free of a core-shell polymer configuration, the second temperature is below the low critical solution temperature of the first monodispersed polymer, the second temperature at about 21°, mixing the isolated IPN nanoparticles with a biologically active material at a third temperature, third temperature is below a gelation temperature (Tg) of the IPN nanoparticles in an aqueous mixture, the biologically active material is a drug, and wherein the first polymer and the second polymer in IPN nanoparticles have weight ratio of about 1:1.88. However, Jones et al. teach at 70℃ temperature (the polymerization temperature) polymer interpenetration was low and that polymerization inside the nanoparticles can be hindered (the images suggest that the interface between the two

materials is fairly sharp and not highly interpenetrated, and shell polymerization inside the core particles is sterically hindered due to less solubility and high density of the globular core at 70°C during polymerization) (p.8302 1st column end paragraph). Therefore, a person of ordinary skill in the art at the time the invention was made, would have recognized that the interpenetration of the polymer networks is sterically hindered due to the presence of core at 70°C temperature, and would have been motivated to modify the polymerization temperature to below the low critical solution temperature of the polymer, in the method as taught by Jones et al. to increase the interpenetration of the polymer networks (less core-shell polymer configuration).

It must be noted that according to Gan et al. poly(N-isopropylacrylamide) (p-NIPA) the polymer used in the method of Jones et al. is poorly soluble in water above the lower critical solution temperature, which cause the core particles to collapse and hinder the penetration of the growing shell during the second stage of the polymerization at 70°C (see page 7513 Results lines 13-19). Therefore, a person of ordinary skill in the art at the time the invention was made would have recognized that the temperature of the polymerization in Jones et al. method is a result-effective-variable and could have been optimized.

Moreover, Kurisawa et al. teach using interpenetrating polymer network (IPN)-structured hydrogels as a drug microreservoir (as a model of a drug substrate), and phase morphology in the IPN-structured hydrogels was varied with the preparation temperature, i.e. above or below the sol-gel transition temperature (T_{trans}) of gelatin (Abstract, and p.194 2nd column 1st paragraph). Kurisawa et al. teach the IPN-structured

hydrogels were prepared below or above the T_{trans} of gelatin and their enzymatic degradability was examined. Dual-stimuli-responsive degradation was achieved in the IPN-structured hydrogels were prepared below T_{trans} having increased miscibility and the dual-stimuli-responsive degradation of Gtn-Dex hydrogels was closely related to the miscibility between Gtn and Dex networks (p.192, 1st column last paragraph and 2nd column 1st paragraph). Kurisawa et al. further teach regulated LM release was achieved in the IPN-structured hydrogel prepared below the T_{trans}, and although LM release from IPN-structured hydrogel prepared above the T_{trans} was observed, the difference in the LM release behavior is though to be have been caused by enzymatic degradability of the hydrogels, being closely related to physical chain entanglements between chemically different polymer networks (p.199 2nd column last paragraph, Conclusion).

Cai et al. teach inside IPN hydrogels, each network may retain its own properties, whereas the proportions of the networks are varied independently. The combined properties of the IPNs can be controlled by the ratios of their component monomers (p.170, 2nd column 2nd paragraph).

Therefore, a person of ordinary skill in the art at the time the invention was made, recognizing that poly(N-isopropylacrylamide) (p-NIPA) used in the Jones et al. is poorly soluble in water above the lower critical solution temperature, would have been motivated to modify the method as taught by Jones et al. by optimizing and lowering the temperature to below the low critical solution temperature of the first monodispersed polymer in order to provide a method of preparing a dispersion of hydrogel nanoparticles and an dispersion of hydrogel nanoparticles with a reasonable

expectation of success in providing a polymer networks which have more interpenetrated structure (substantially free of core-shell polymer configuration). Because Gan et al. teach poly(N-isopropylacrylamide (the polymer used in the Jones et al.) is poorly soluble in water above the lower critical solution temperature, which cause the core particles to collapse and hinder the penetration of the growing shell during the second stage of the polymerization. Moreover, a person of ordinary skill in the art at the time the invention was made would have been motivated to modify the method and the dispersion of hydrogel nanoparticles as taught by Jones et al. by adding a drug at a third temperature below a gelation temperature of the IPN nanoparticles in an aqueous mixture, according to the teachings of Kurisawa et al. with a reasonable expectation of success, because Kurisawa et al. teach IPN-structured hydrogels can be prepared below the T_{trans}, and drug release using IPN-structured hydrogel prepared below gel transition temperature.

Accordingly, since the ratio of the first polymer to the second polymer in the IPN nanoparticles is a variable that depends on the amounts (or ratio) of the monomers being mixed (a result-effective variable), therefore this ratio in the method as taught by Jones et al. could have been optimized by routine experimentation at the time of the invention by a person of ordinary skill in the art, said person recognizing that the phase transition properties of the IPNs can be controlled by the ratios of their component monomers. The motivation as taught by Jones would be to provide a dispersion of IPN nanoparticles with less complex phase transition behavior.

Claims 29-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones et al. (Macromolecules, 2000, Vol. 33, p.8301-8306) in view of Cai et al. (Journal of Applied Polymer Science, 2002, Vol. 83, p.169-178) and further in view of Hennink & Nostrum (Advanced Drug Delivery Reviews, 2002, Vol. 54, p.13-36).

Claims 29-47 are drawn to a method of preparing a nanocluster of cross-linked IPN nanoparticles comprising, providing a dispersion of IPN nanoparticles, adding a first cross linking agent and a second cross linking agent to the dispersion of the IPN nanoparticles, heating the IPN cross linking solution to a first temperature for a period of time, wherein the IPN nanoparticles have uniformed size and comprise a first polymer network interpenetrating a second polymer network, mixing the nanocluster of cross-linked IPNs with a biologically active material at a second temperature, the first polymer comprises of poly(-N-isopropylacrylamide) and the second polymer comprises poly(acrylic acid), first cross-linking agent comprises EDAC and second cross linking agent comprises adipic acid dihydrazide, heating at a first temperature, about 44°C, for about 25-45 min (33-37 min), mixing cross-linked IPNs with a biologically active material at about 33°C, and hydrodynamic radius in the range from 225 nm to about 240 nm, a nanocluster of cross-linked IPN nanoparticles comprising: at least two IPN nanoparticles linked by a cross-linking group, a first polymer network interpenetrating a second polymer network, the cross linking group is adipic acid dihydrazide, wherein each IPN nanoparticles have a uniformed sized and an have an average hydrodynamic radius of nanoparticles is in the range of 155 nm to about 1000 nm.

As mentioned immediately above, Jones et al. teach providing a dispersion of IPN nanoparticles. Jones et al. teach preparing an aqueous dispersion/hydrogels of IPN nanoparticles, the first polymer comprises of poly(-N-isopropylacrylamide) and the second polymer comprises poly(acrylic acid), the IPN nanoparticles have an average hydrodynamic radius is in the range of 75 nm to about 200 nm, and heating at a first temperature about 44°C, for about 25-45 min (30 minutes) (p.8302 2nd column Figure 2. radius vs. Temp graph, b. Y-axis, radius of particles 80-200 nm). Jones et al. also teach change in the particle size of the aqueous dispersion around 30 nm (at pH 6.5) when it is heated from below a volume phase transition temperature to above a volume transition temperature (about 34°C), the magnitude of the particle (p. 8304 Figure 5, Deswelling curves for particle at pH 6.5, the 1st curve on the top, radius change around 34°C, decrease in the magnitude of the particle size change, and the temperature on y-axis of the graph, and p. 8303 2nd column 3rd paragraph lines 13-15).

Jones et al. do not teach cross linking a dispersion of IPN nanoparticles, IPN nanoparticles are substantially free of a core-shell polymer configuration, and the first cross-linking agent comprises EDAC and second cross linking agent comprises adipic acid dihydrazide, mixing the nanocluster with a biologically active molecule at a second temperature. However, as mentioned immediately above, at the time the invention was made it was well known in the art that poly (N-isopropylacrylamide (the polymer used in the Jones et al.) was poorly soluble in water above the lower critical solution temperature, which would cause the core particles to collapse and hindered the penetration of the growing shell during the second stage of the polymerization at 70°C.

Therefore, a person of ordinary skill in the art at the time the invention was made would have recognized that the polymerization conditions including the temperature of the polymerization were result-effective-variable and would be optimized in order to increase the interpenetration of the polymer networks (less core-shell polymer configuration) in the method and hydrogel nanoparticles of Jones et al., in the absence of evidence to the contrary.

Moreover, Cai et al. teach a method of preparing a nanocluster of cross-linked nanoparticles and a nanocluster of cross-linked nanoparticles (Abstract, and p. 172 2nd column end paragraph line 2). Cai et al. teach the nanoparticles are ionic particles because of the carboxylic charge on acrylic acid (AA), in these microgel particles the AA groups tend to lie on the surface of the particles, and NIPAAm groups lie toward the inside, this prevents aggregation between microgel particles and makes the microgel particles stable in the aqueous solutions. In this conformation, the carboxyl groups of on the microgel particle surface can also be further cross-linked under suitable conditions, forming interpenetrating network structure (p.172 2nd column last paragraph and p.173 1st column). Cai et al. further teach mixing the particles with a biologically active material (bovine serum albumin, a protein) at different temperatures (p.172, 2nd column 1st paragraph). Cai et al. teach to increase the volume and surface area of the bulk hydrogels, hydrogels can be synthesized at temperatures above the LCST of the polymer by heating the reaction near the end of the polymerization (p.169 2nd column last paragraph).

Furthermore, Hennink & Nostrum teach cross-liking agents EDC (or EDAC) is a highly efficient reagent to crosslink water-soluble polymers with amide bonds, and hydrogel formation by using a less toxic cross linking agent adipic acid dihydrazide in the presence of a drug, for aldehyde-mediated crosslinking (p.20 1st column 2nd paragraph) (p.19, 1st column lines 20-23).

Therefore, a person of ordinary skill in the art at the time the invention was made would have been motivated to apply the prior art teachings and to use the method of Cai et al. to cross-link the dispersion of IPN nanoparticles of Jones et al. with the predictable results of preparing a nanocluster of cross-linked IPN nanoparticles and a nanocluster of cross-liked IPN nanoparticles because Cai et al. teach cross-linking nanoparticles to form a larger hydrogel/nanocluster. The motivation would be to create a larger network structure.

Moreover, a person of ordinary skill in the art at the time the invention was made, would have been motivated to use the cross-liking agents EDC and adipic acid dihydrazide as taught by Hennink & Nostrum to cross-link the dispersion of IPN nanoparticles according to the teachings of Cai et al. with the predictable results of preparing a nanocluster of cross-linked IPN nanoparticles and a nanocluster of cross-liked IPN nanoparticles, because Hennink & Nostrum teach EDC and adipic acid dihydrazide can be used to form hydrogels. The motivation as taught by Hennink & Nostrum would be to cross-link different functional groups, and low toxicity of adipic acid dihydrazide.

Answer to Arguments

Applicant's arguments filed on 04/29/2010 have been fully considered but they are not persuasive.

With respect to the rejection of claims 1-7 and 11-28 under 35 U.S.C. 103(a) as being unpatentable over Jones et al., and the rejection of claims 29-47 under 35 U.S.C. 103(a) as being unpatentable over Cai et al. Applicant's arguments are considered but are not persuasive.

Applicant argues that Jones reference teaches preparation of core-shell hydrogel nanoparticles therefore it teaches away from IPN nanoparticles that are substantially free of core-shell polymer configuration. This is not found persuasive because as mentioned immediately above, the amendment to claims 1, 29 and 41 introduces new matter to the specification. Applicant should also specifically point out the support for any amendments made to the disclosure. See MPEP § 2163.06.

Moreover, Jones et al. do not teach away form IPN nanoparticles that are substantially free from core-shell configuration since Jones et al. disclosure does not criticize, discredit, or otherwise discourage preparing the claimed IPN nanoparticles that are a substantially free from core-shell configuration.

Therefore, a person of ordinary skill in the art at the time the invention was made, recognizing that poly(N-isopropylacrylamide) of Jones et al. is poorly soluble in water above the lower critical solution temperature, would have been motivated to modify the method as taught by Jones et al. by optimizing and lowering the temperature to below the low critical solution temperature of the first (monodispersed) polymer in order to provide a method of preparing a dispersion of hydrogel nanoparticles and an dispersion

of hydrogel nanoparticles with a reasonable expectation of success in providing a polymer networks which have more interpenetrated structure (substantially free of core-shell polymer configuration). Because Gan et al. teach poly(N-isopropylacrylamide (the polymer used in the Jones et al.) is poorly soluble in water above the lower critical solution temperature, which cause the core particles to collapse and hinder the penetration of the growing shell during the second stage of the polymerization.

Accordingly Applicant claims a combination that only unites old elements with no change in the respective functions of those old elements, and the combination of those elements yields predictable results; absent evidence that the modifications necessary to effect the combination of elements is uniquely challenging or difficult for one of ordinary skill in the art, the claim is unpatentable as obvious under 35 U.S.C. 103(a).
Ex Parte Smith, 83 USPQ.2d at 1518-19 (BPAI, 2007) (citing KSR, 127 S.Ct. at 1740, 82 USPQ2d at 1396).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kade Ariani whose telephone number is (571) 272-6083. The examiner can normally be reached on IFP.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kade Ariani/
Examiner, Art Unit 1651